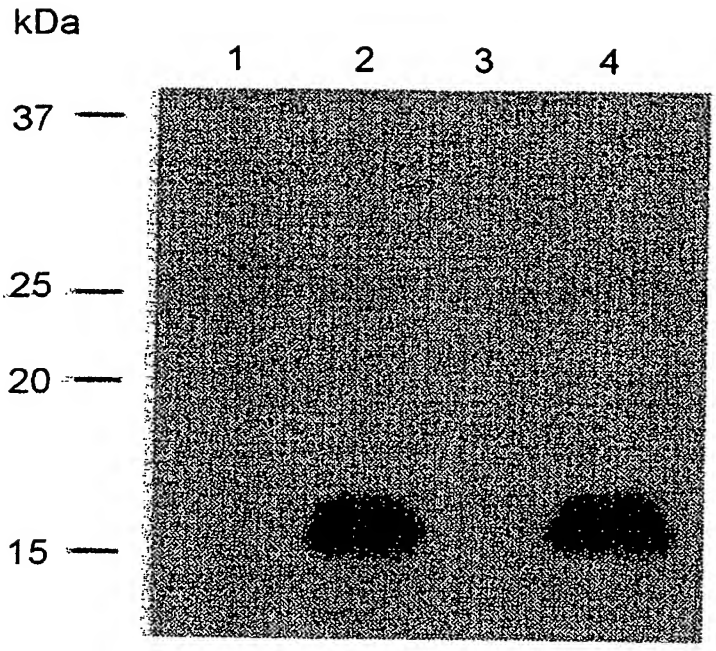


Figure 1

BEST AVAILABLE COPY

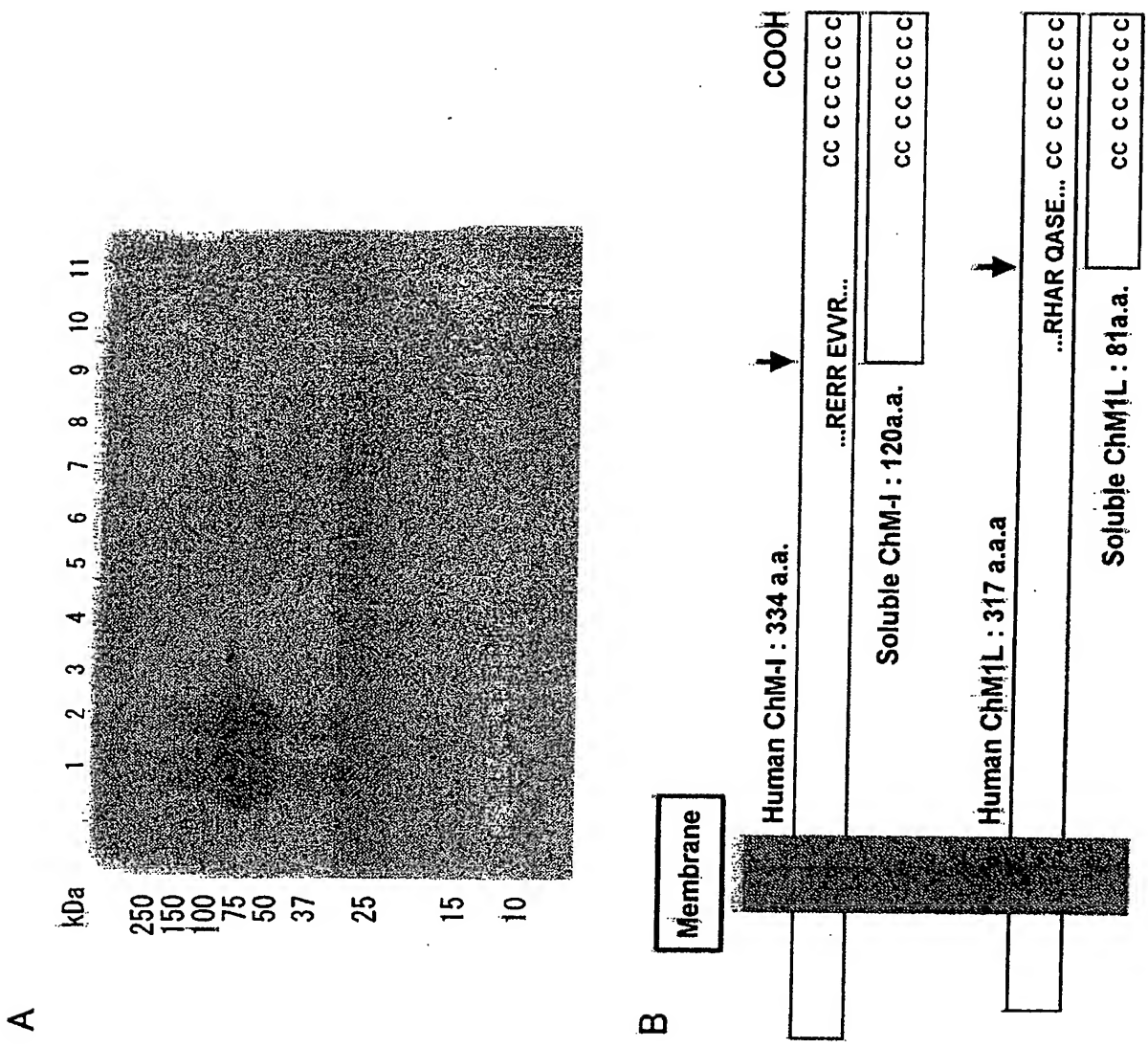

A
kDa
250
150
100
75
50
37
25
15
10
1 2 3 4 5 6 7 8 9 10 11
B
Membrane
Human ChM-I : 334 a.a.
COOH
...RERR EVVR...
cc cccccc
Soluble ChM-I : 120a.a.
cc cccccc
Human ChM1L : 317 a.a.a
...RHAR QASE...
cc cccccc
Soluble ChM1L : 81a.a.
cc cccccc

Figure 2

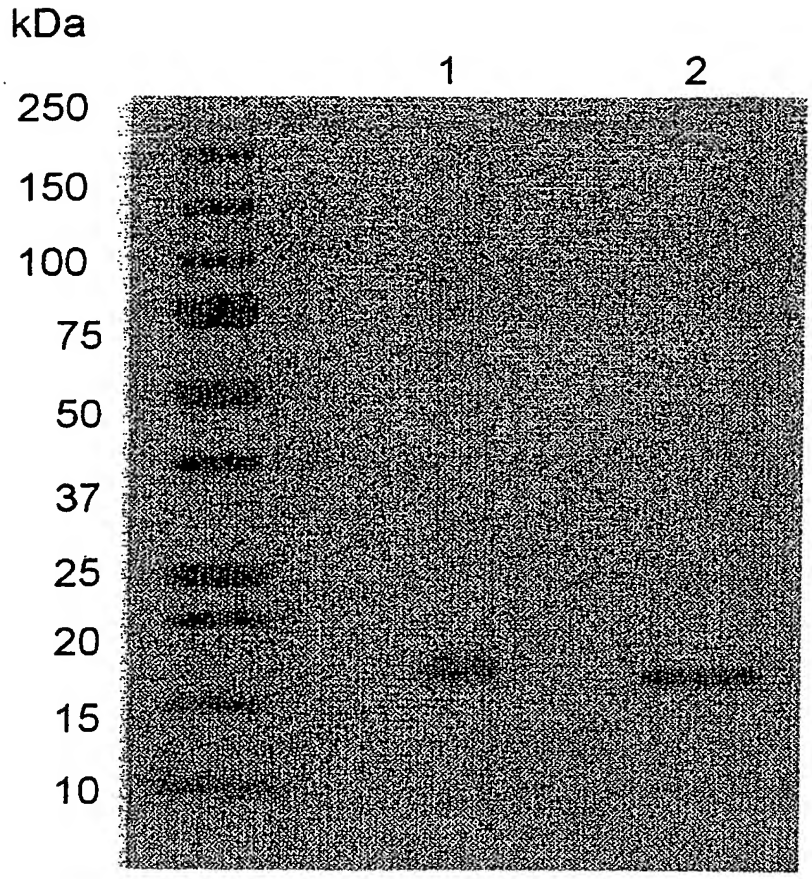


Figure 3

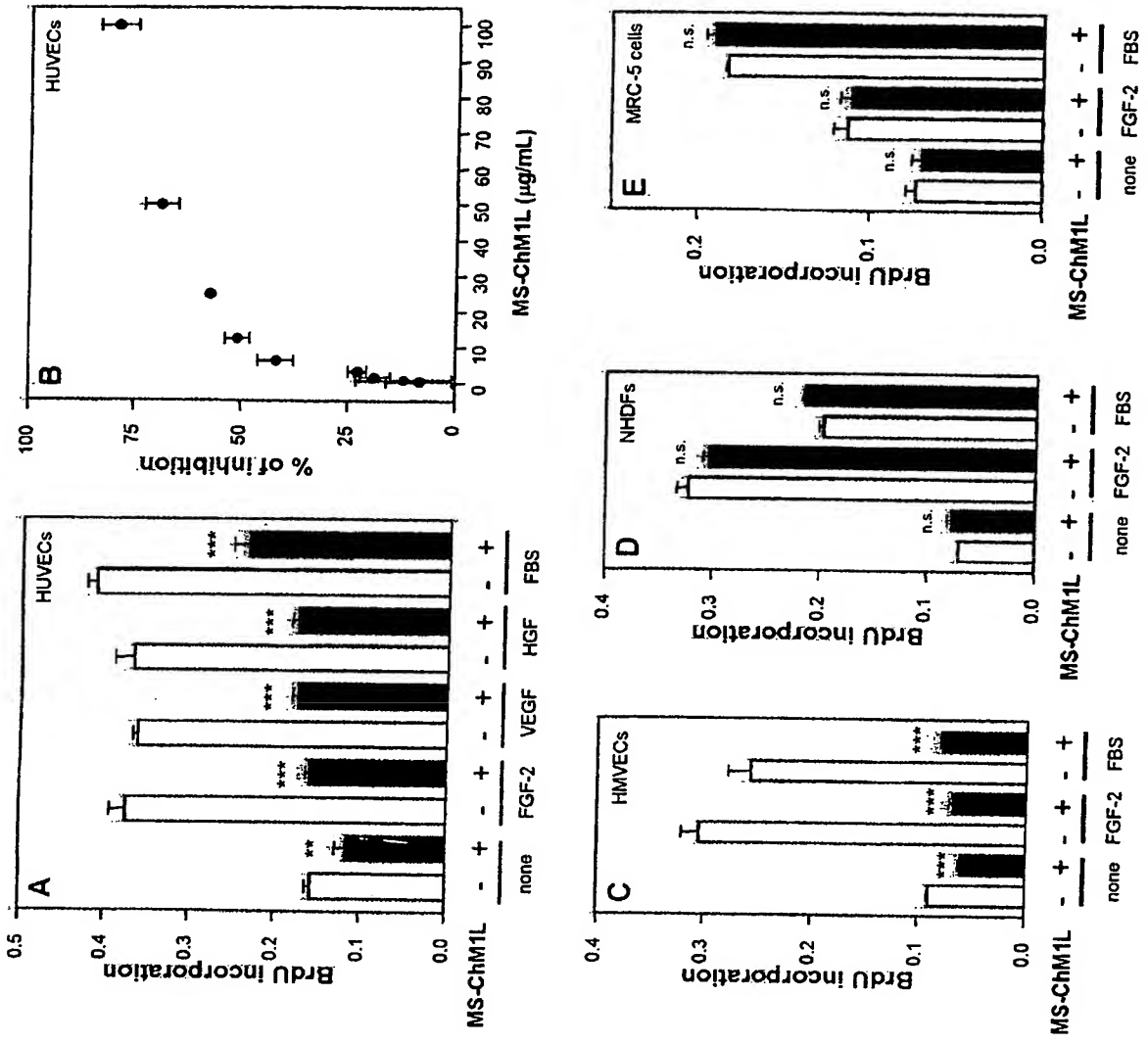

A
HUVECs
BrdU incorporation
MS-ChM1L
none
FGF-2
VEGF
HGF
FBS
B
HUVECs
% of inhibition
MS-ChM1L (µg/mL)
C
HMVECs
D
NHDFs
E
MRC-5 cells
n.s.

Figure 4

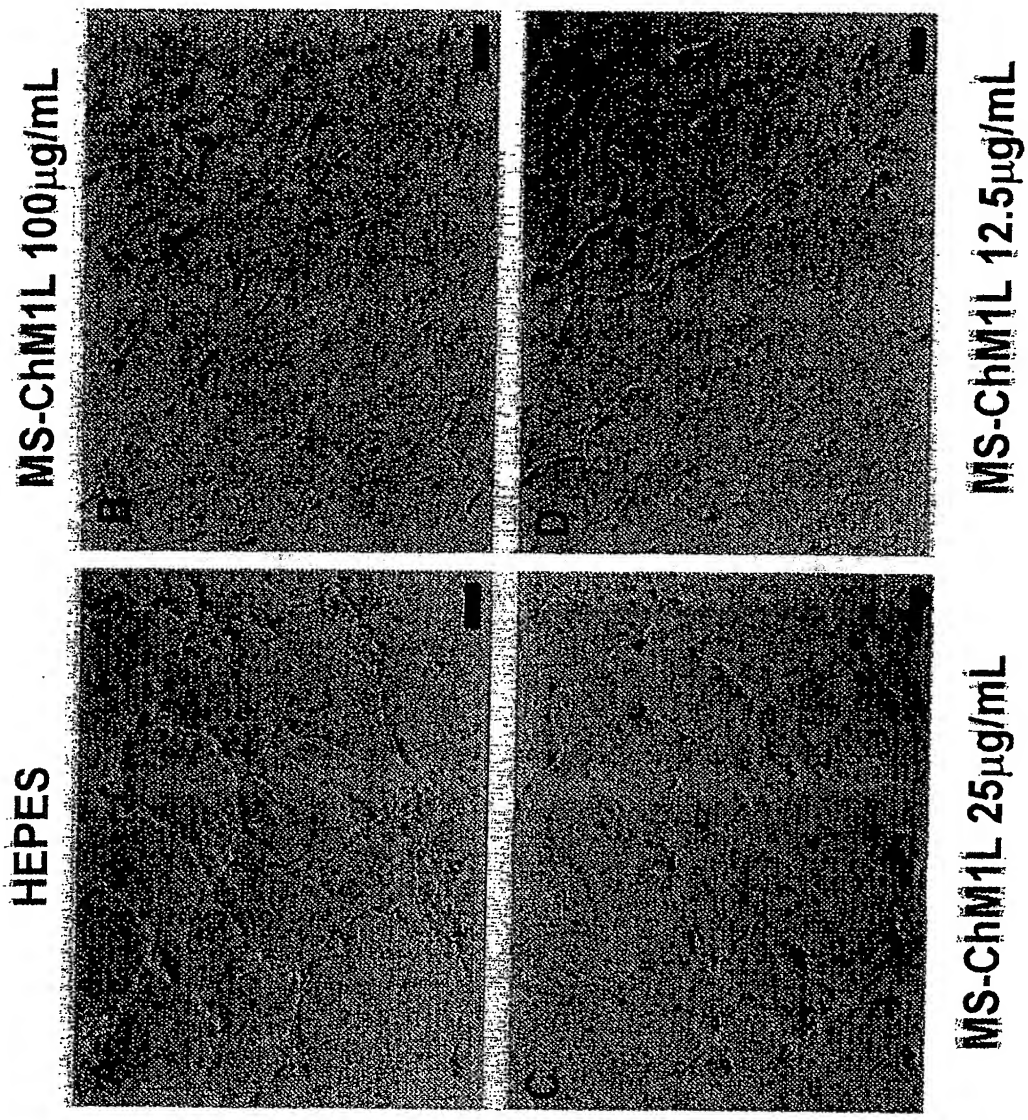


Figure 5

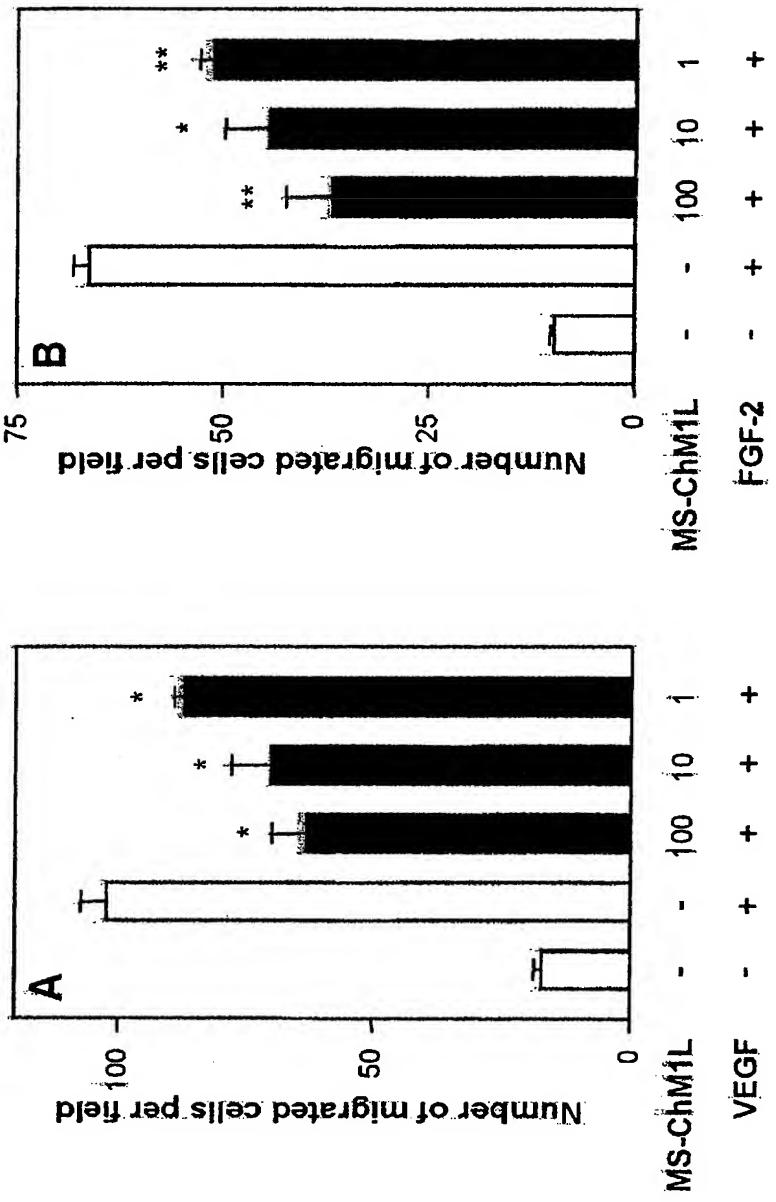

A
Number of migrated cells per field
0
50
100
MS-ChM1L - - 100 10 1
VEGF - + + + +
*
B
Number of migrated cells per field
0
25
50
75
MS-ChM1L - - 100 10 1
FGF-2 - + + + +
**
*
**

Figure 6

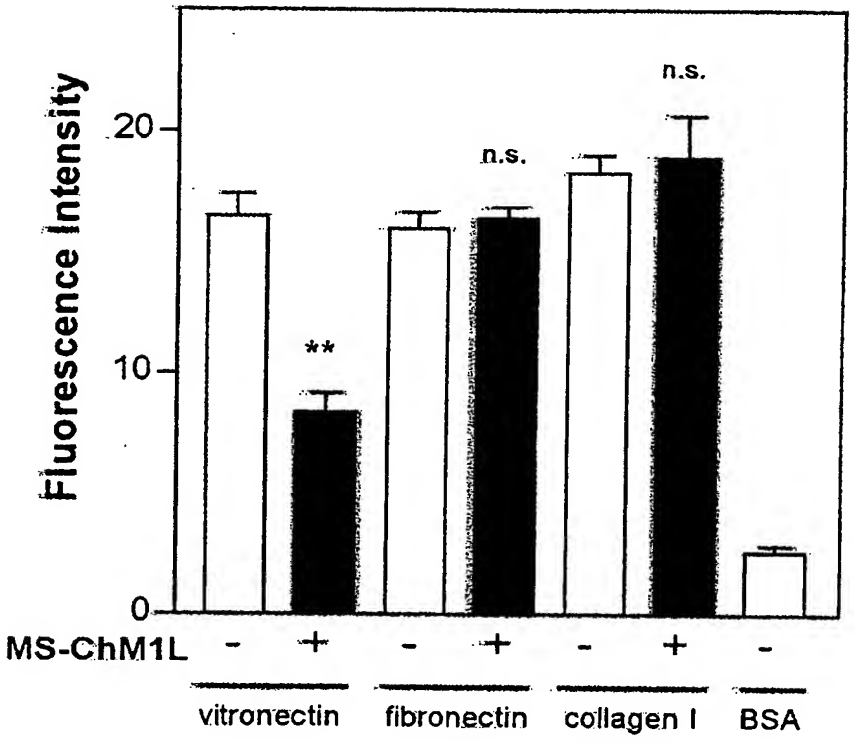

Fluorescence Intensity
20
10
0
n.s.
n.s.
**
MS-ChM1L - + - + - + -
vitronectin
fibronectin
collagen I
BSA

Figure 7

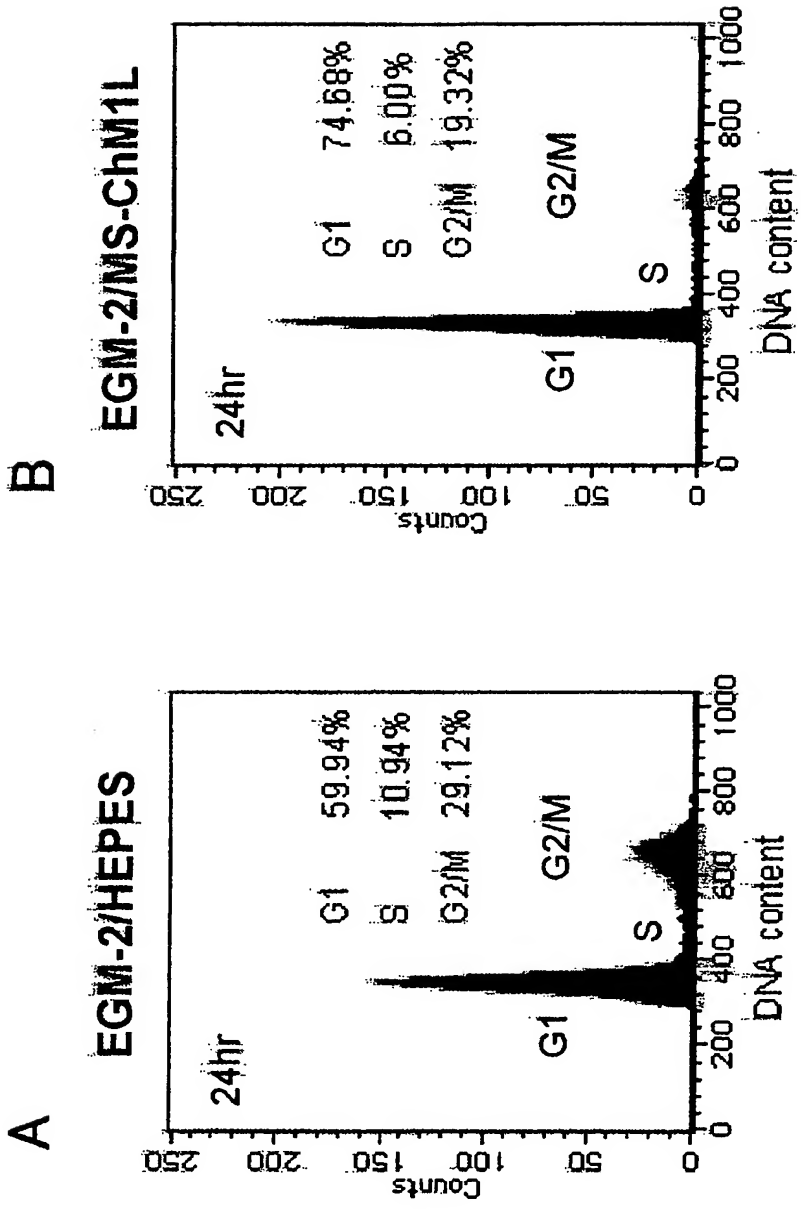

A
EGM-2/HEPES
24hr
G1 59.94%
S 10.94%
G2/M 29.12%
G1
S
G2/M
Counts
DNA content
B
EGM-2/MS-ChM1L
24hr
G1 74.68%
S 6.00%
G2/M 19.32%
G1
S
G2/M
Counts
DNA content

Figure 8

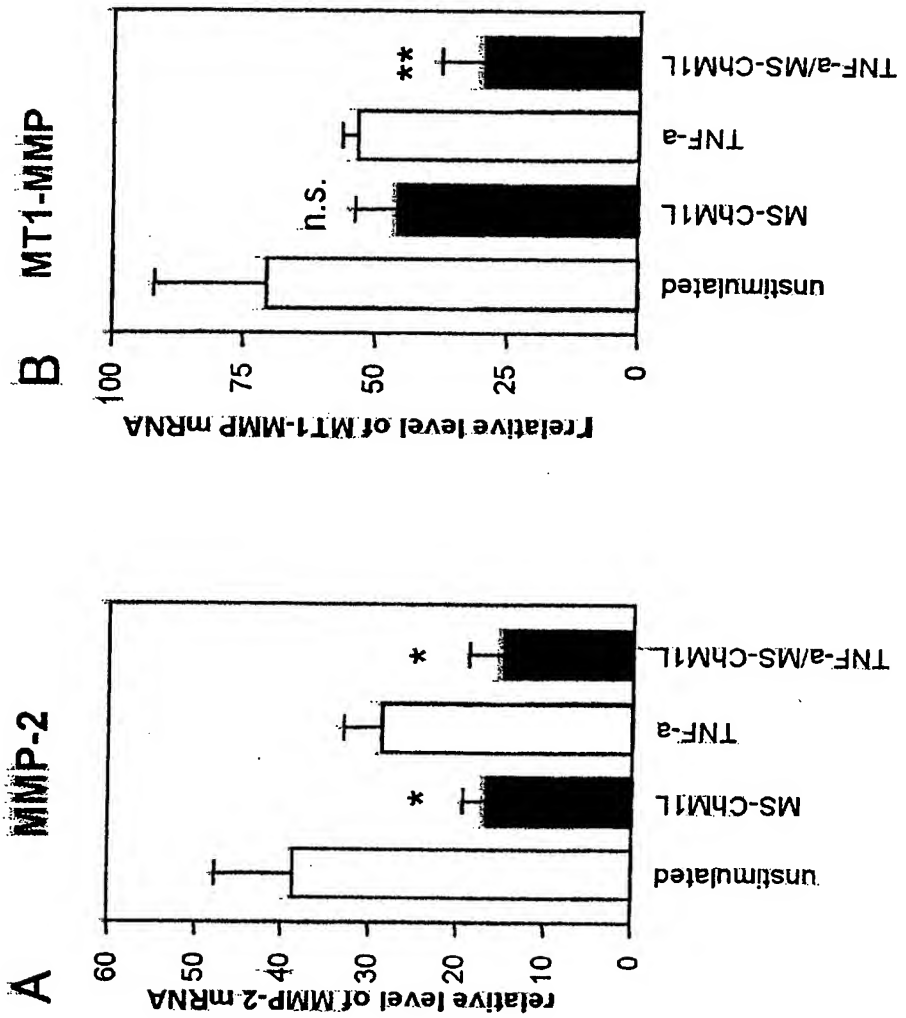

B
MT1-MMP
Relative level of MT1-MMP mRNA
100
75
50
25
0
n.s.
**
unstimulated
MS-ChM1L
TNF-a
TNF-a/MS-ChM1L
A
MMP-2
relative level of MMP-2 mRNA
60
50
40
30
20
10
0
*
*
unstimulated
MS-ChM1L
TNF-a
TNF-a/MS-ChM1L

Figure 9

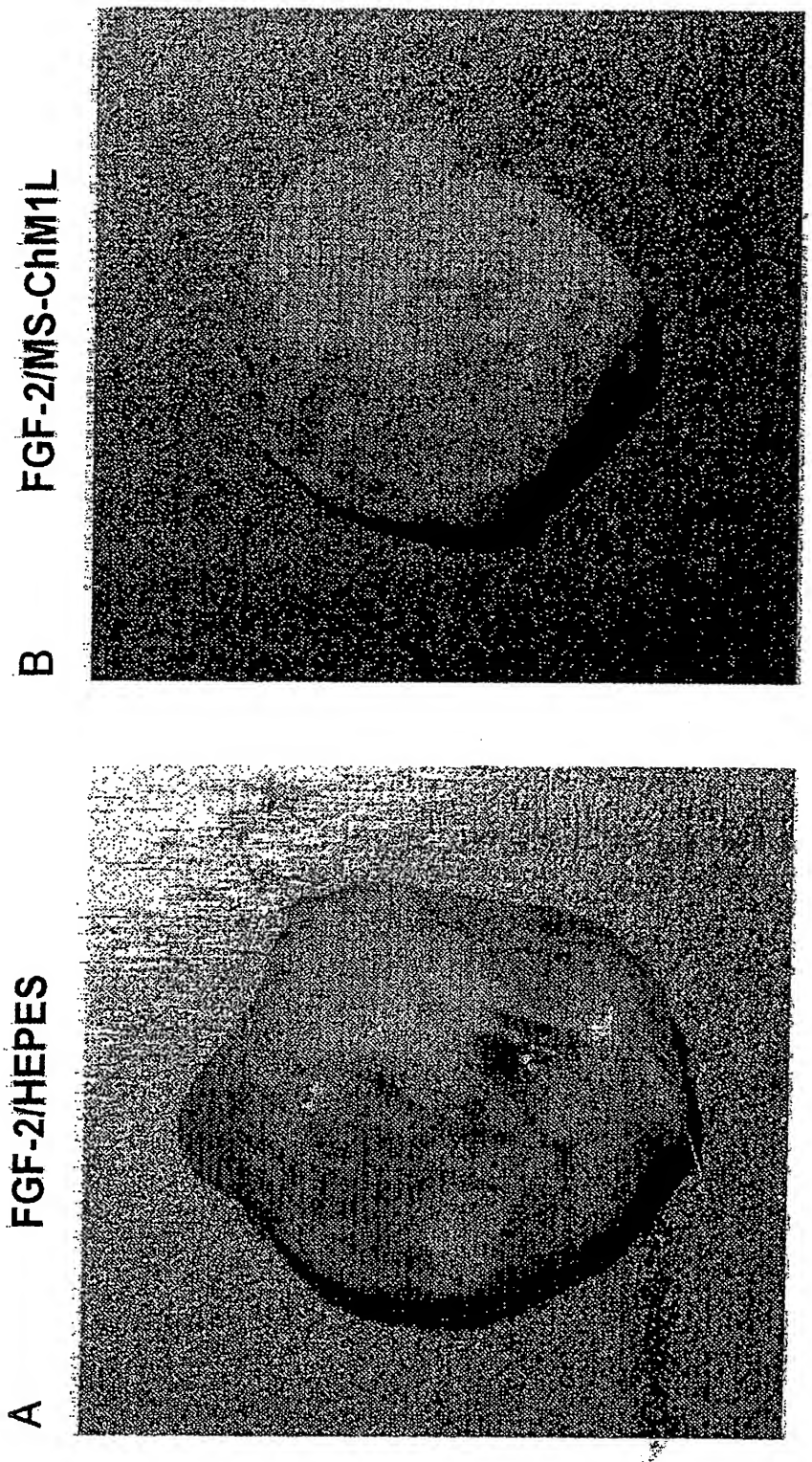


Figure 10

A: M-CSF 100 ng/mL

B: M-CSF 100 ng/mL
+ RANKL 50 ng/mL
+ Vehicle

C: M-CSF 100 ng/mL
+ RANKL 50 ng/mL
+ MS-ChM1L 10 μg/mL

D: M-CSF 100 ng/mL
+ RANKL 50 ng/mL
+ MS-ChM1L 100 μg/mL

E: M-CSF 100 ng/mL
+ RANKL 50 ng/mL
+ ChM-I 10 μg/mL

F: M-CSF 100 ng/mL
+ RANKL 50 ng/mL
+ ChM-I 25 μg/mL

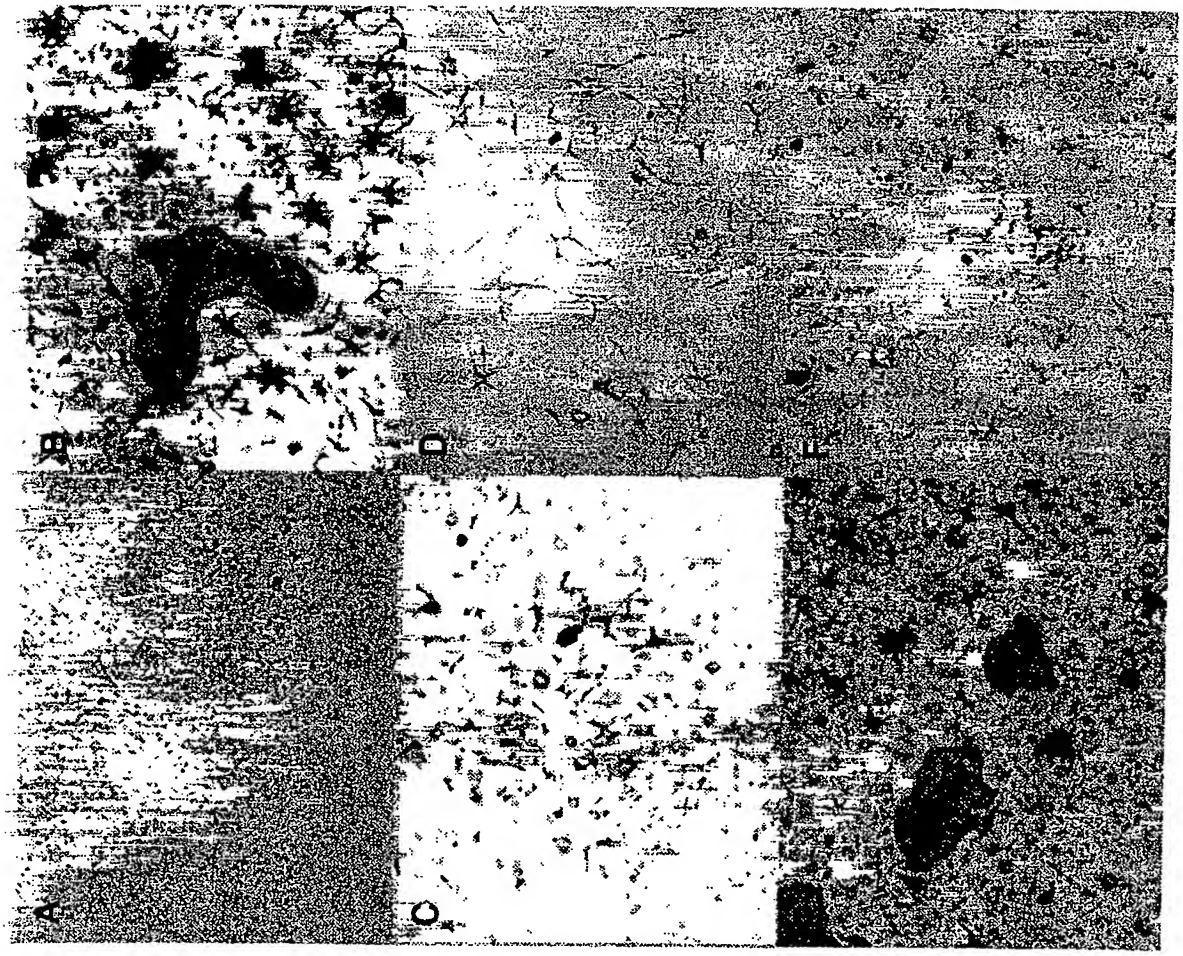


Figure 11

A: 1,25(OH)2D3 (10-8 M)
+ Vehicle
B: 1,25(OH)2D3 (10-8 M)
+ MS-ChM1L 10 μg/mL
C: 1,25(OH)2D3 (10-8 M)
+ MS-ChM1L 100 μg/mL
D: 1,25(OH)2D3 (10-8 M)
+ ChM-I 10 μg/mL
E: 1,25(OH)2D3 (10-8 M)
+ ChM-I 25 μg/mL
A
B
C
D
E

Figure 12

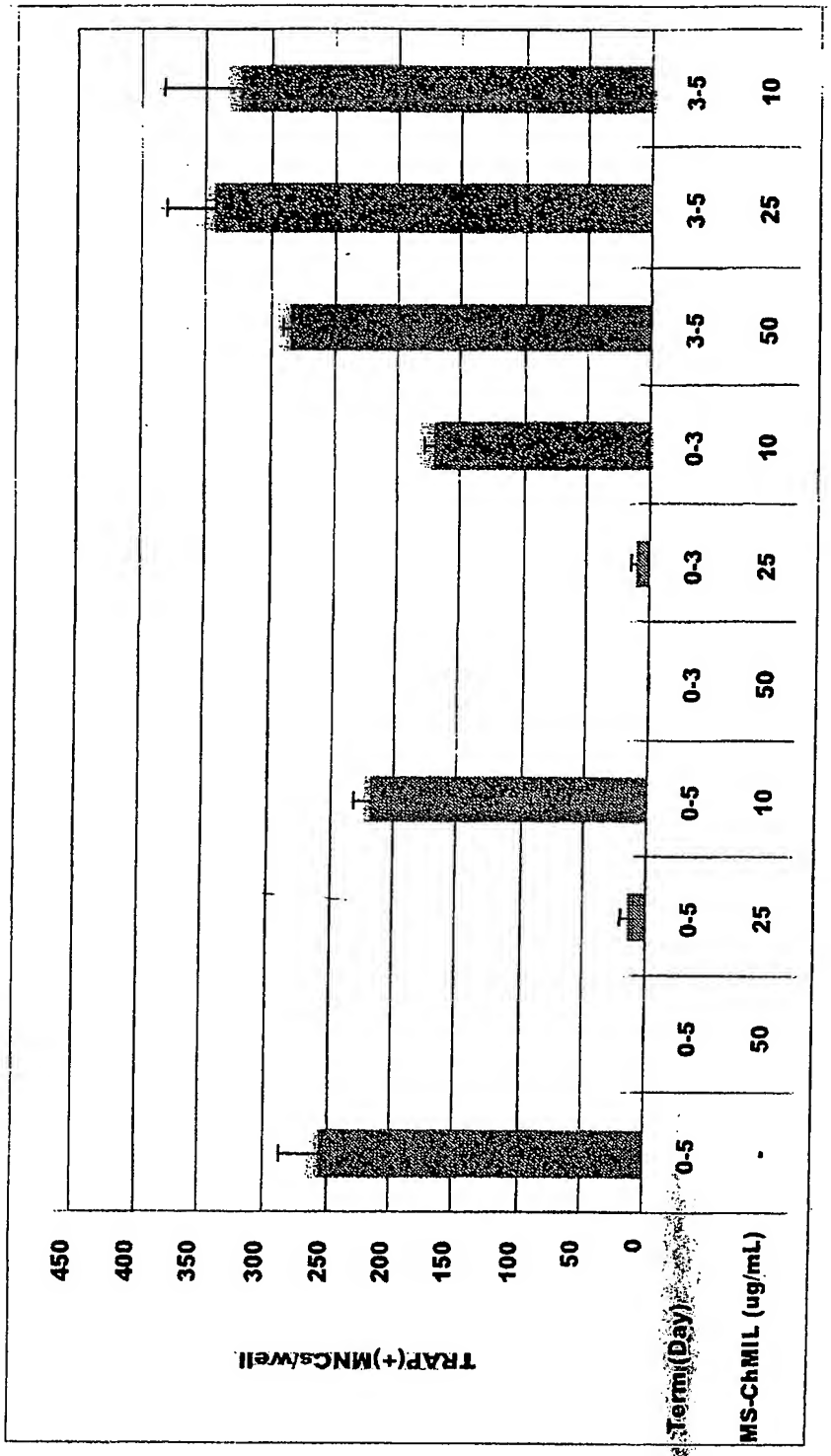

TRAP(+)MNCs/well
450
400
350
300
250
200
150
100
50
0
Term(Day)
MS-ChMIL (ug/mL)
0-5
-
0-5
50
0-5
25
0-5
10
0-3
50
0-3
25
0-3
10
3-5
50
3-5
25
3-5
10

Figure 13

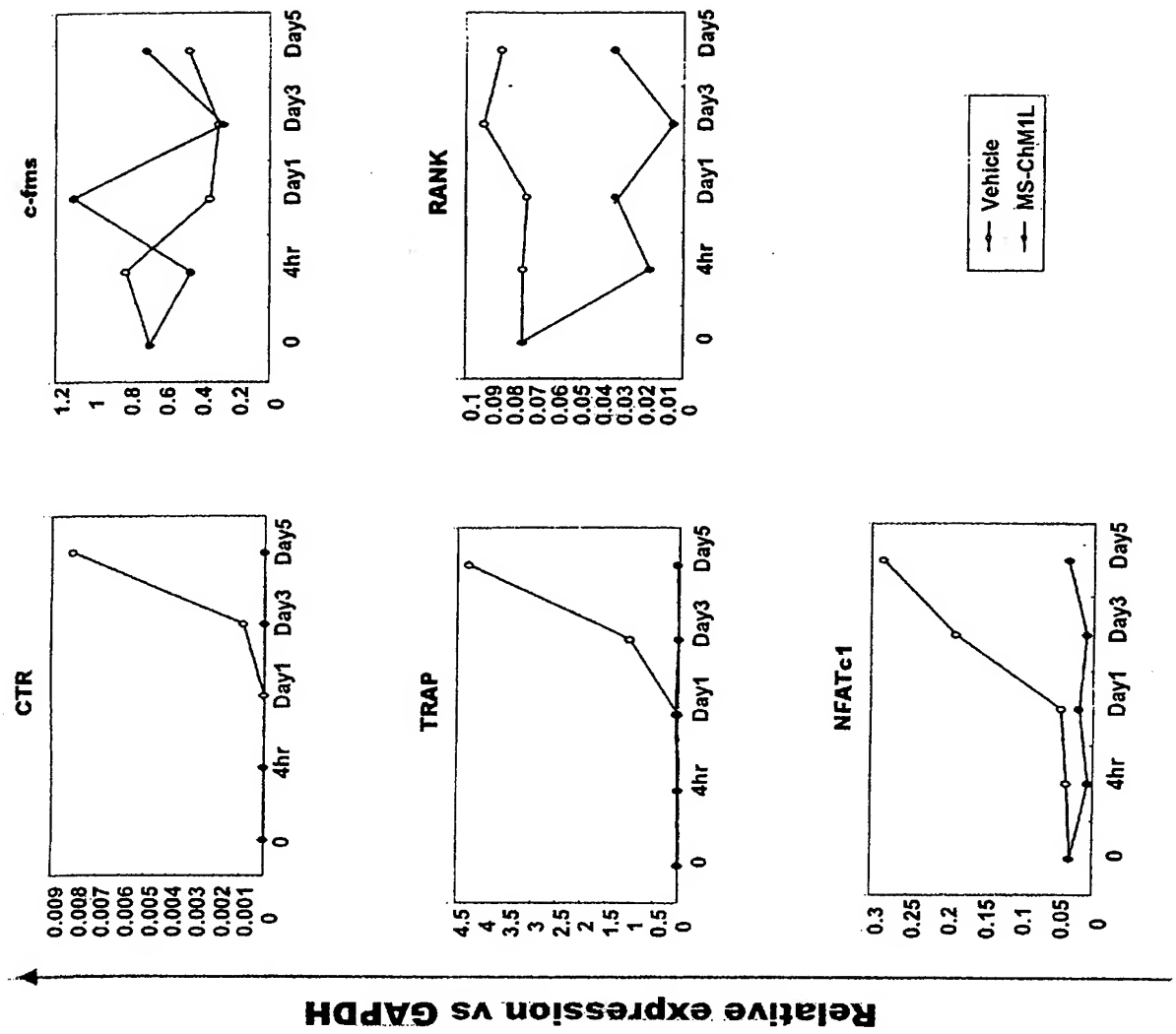

c-fms
RANK
Vehicle
MS-ChM1L
CTR
TRAP
NFATc1
0
4hr
Day1
Day3
Day5
Relative expression vs GAPDH

Figure 14

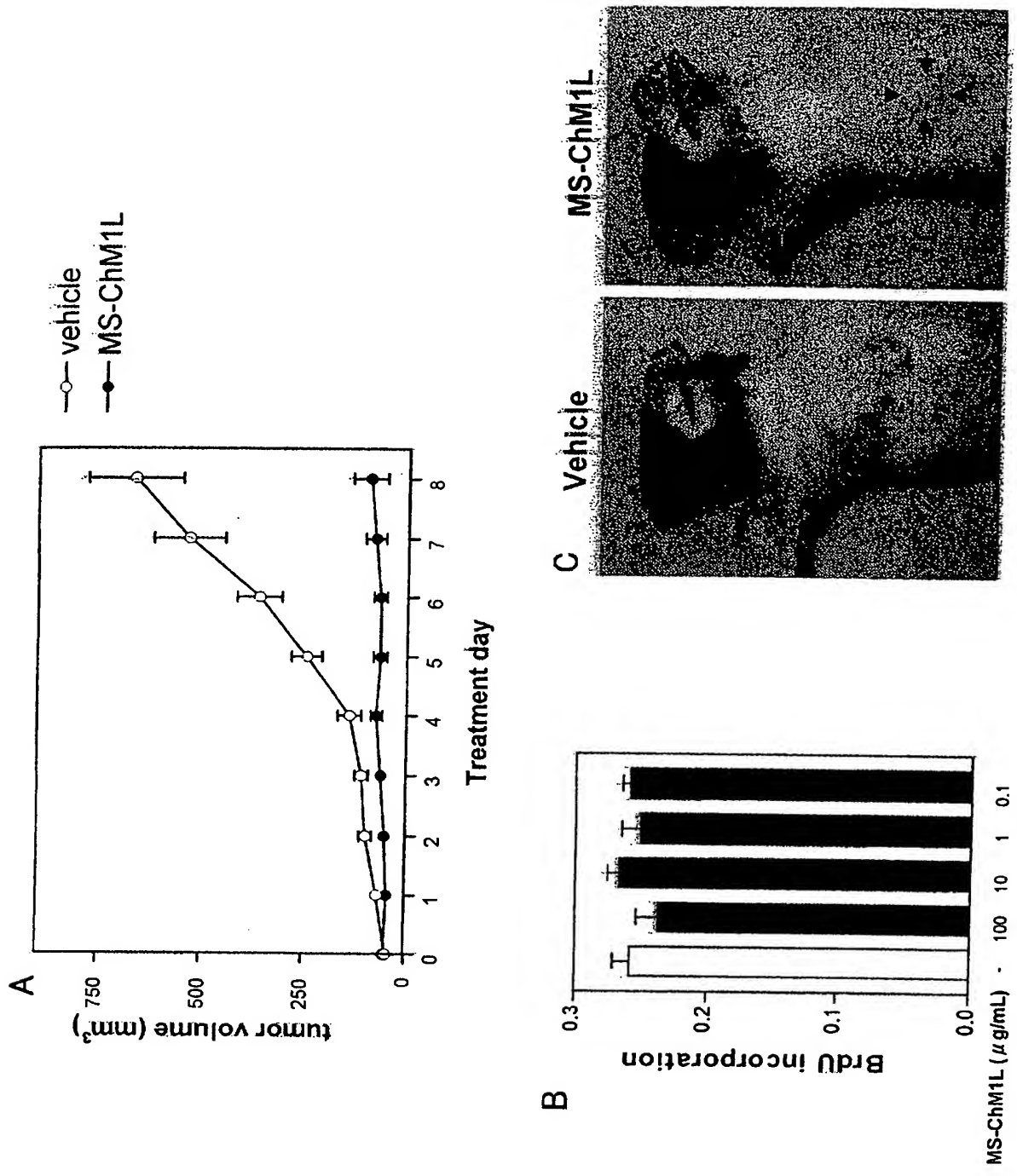

A
vehicle
MS-ChM1L
tumor volume (mm³)
750
500
250
0
0
1
2
3
4
5
6
7
8
Treatment day
B
BrdU incorporation
0.3
0.2
0.1
0.0
MS-ChM1L (μg/mL) -
100
10
1
0.1
C
Vehicle
MS-ChM1L

Figure 15

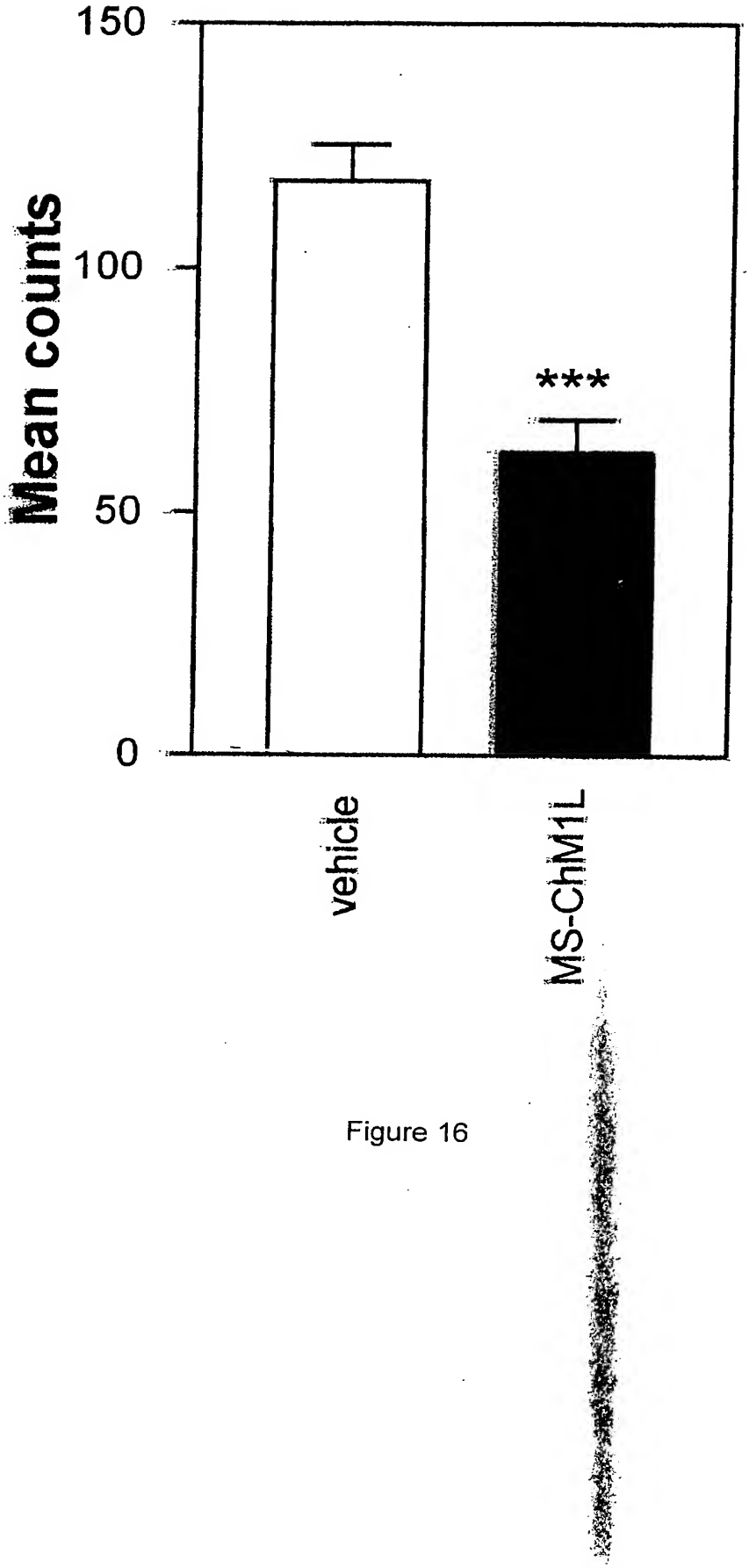


Figure 16

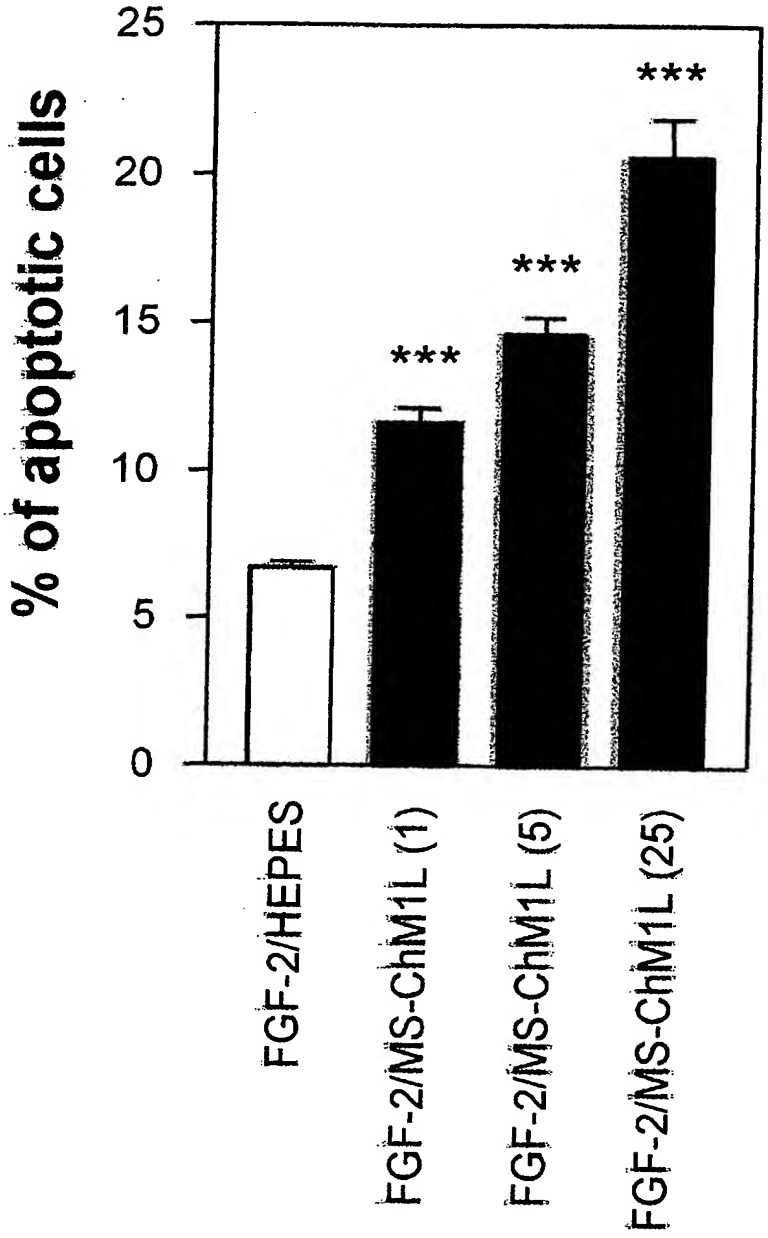

% of apoptotic cells
25
20
15
10
5
0
***
***
***
FGF-2/HEPES
FGF-2/MS-ChM1L (1)
FGF-2/MS-ChM1L (5)
FGF-2/MS-ChM1L (25)

Figure 17

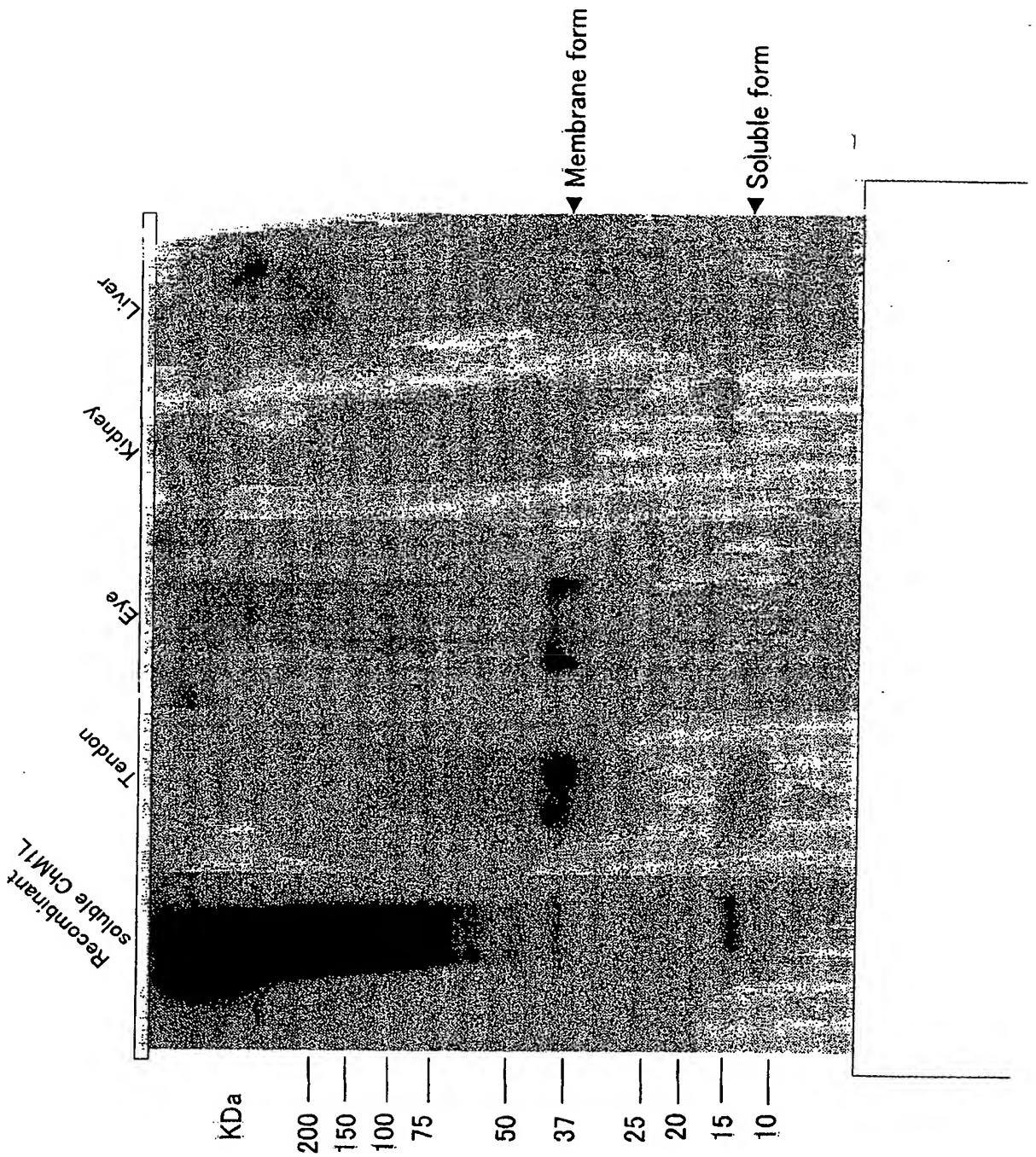

Membrane form
Soluble form
Liver
Kidney
Eye
Tendon
Recombinant soluble ChM1L
KDa
200
150
100
75
50
37
25
20
15
10

Figure 18

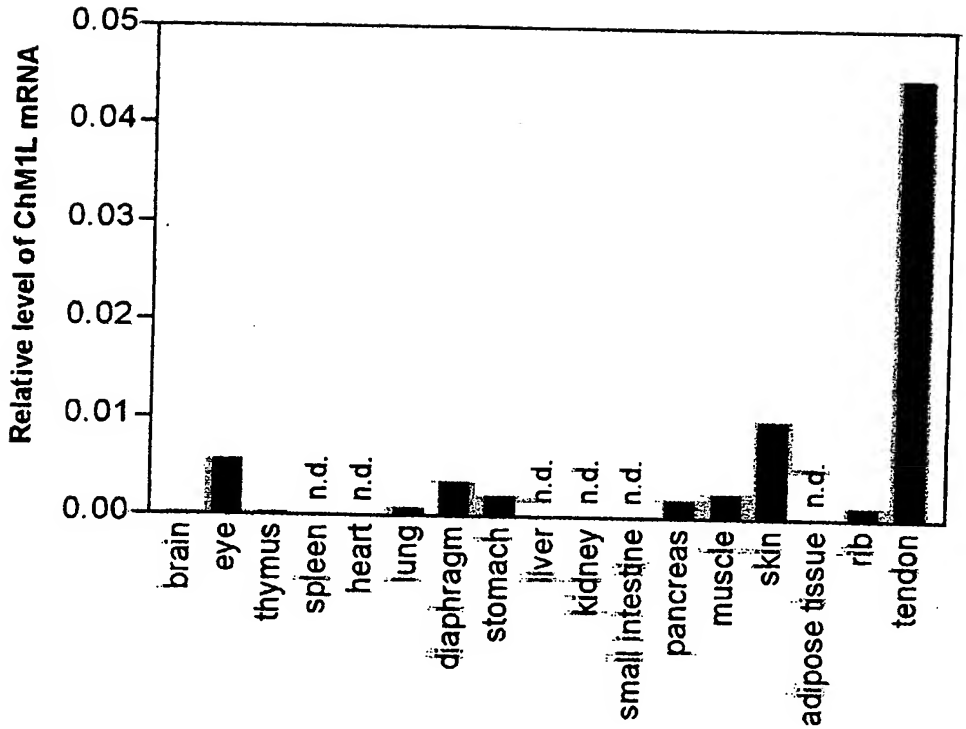

Relative level of ChM1L mRNA
0.05
0.04
0.03
0.02
0.01
0.00
n.d.
n.d.
n.d.
n.d.
n.d.
brain
eye
thymus
spleen
heart
lung
diaphragm
stomach
liver
kidney
small intestine
pancreas
muscle
skin
adipose tissue
rib
tendon

Figure 19

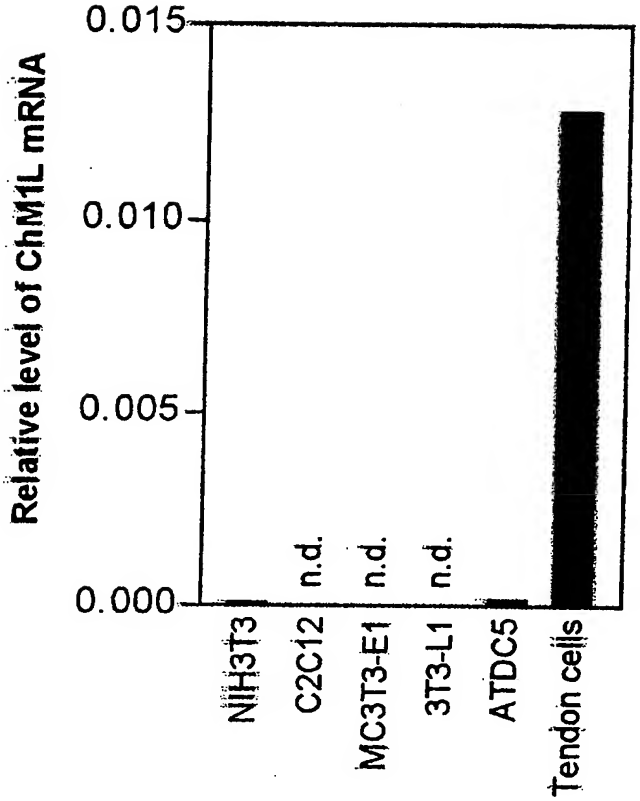
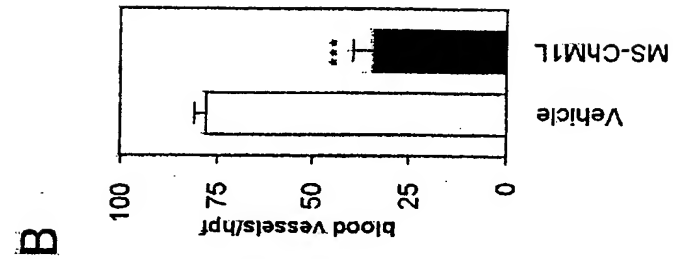

Relative level of ChM1L mRNA
0.015
0.010
0.005
0.000
n.d.
n.d.
n.d.
NIH3T3
C2C12
MC3T3-E1
3T3-L1
ATDC5
Tendon cells

Figure 20


B
blood Vessels/hpf
100
75
50
25
0
***
Vehicle
MS-ChM1L

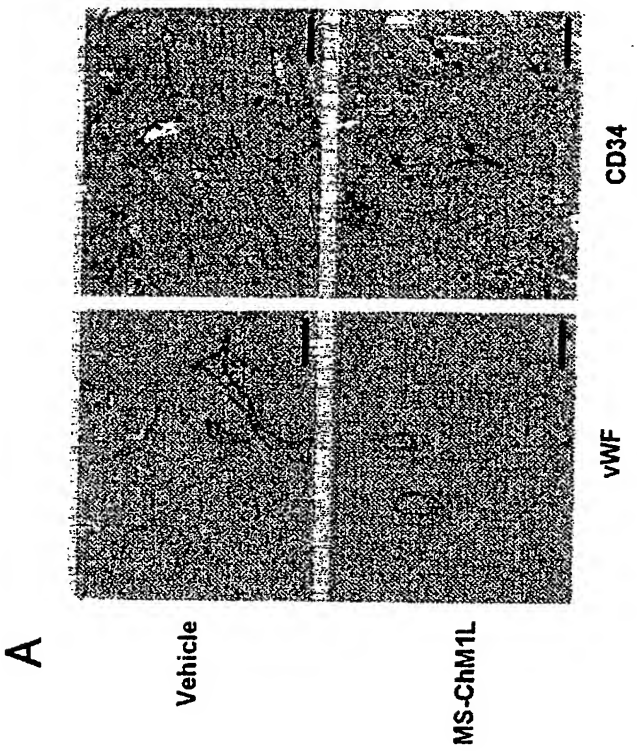

A
Vehicle
MS-ChM1L
vWF
CD34

Figure 21

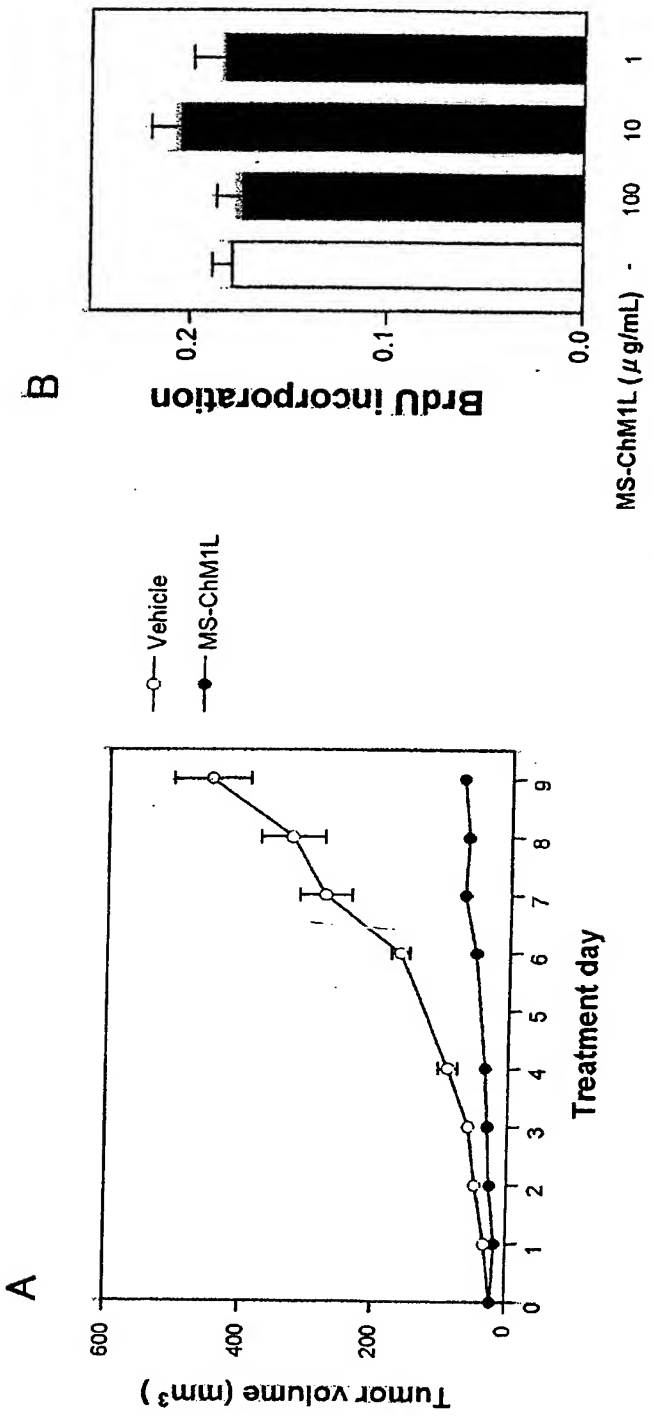

A
Tumor volume (mm³)
600
400
200
0
0 1 2 3 4 5 6 7 8 9
Treatment day
Vehicle
MS-ChM1L
B
BrdU incorporation
0.2
0.1
0.0
MS-ChM1L (μg/mL) - 100 10 1

Figure 22

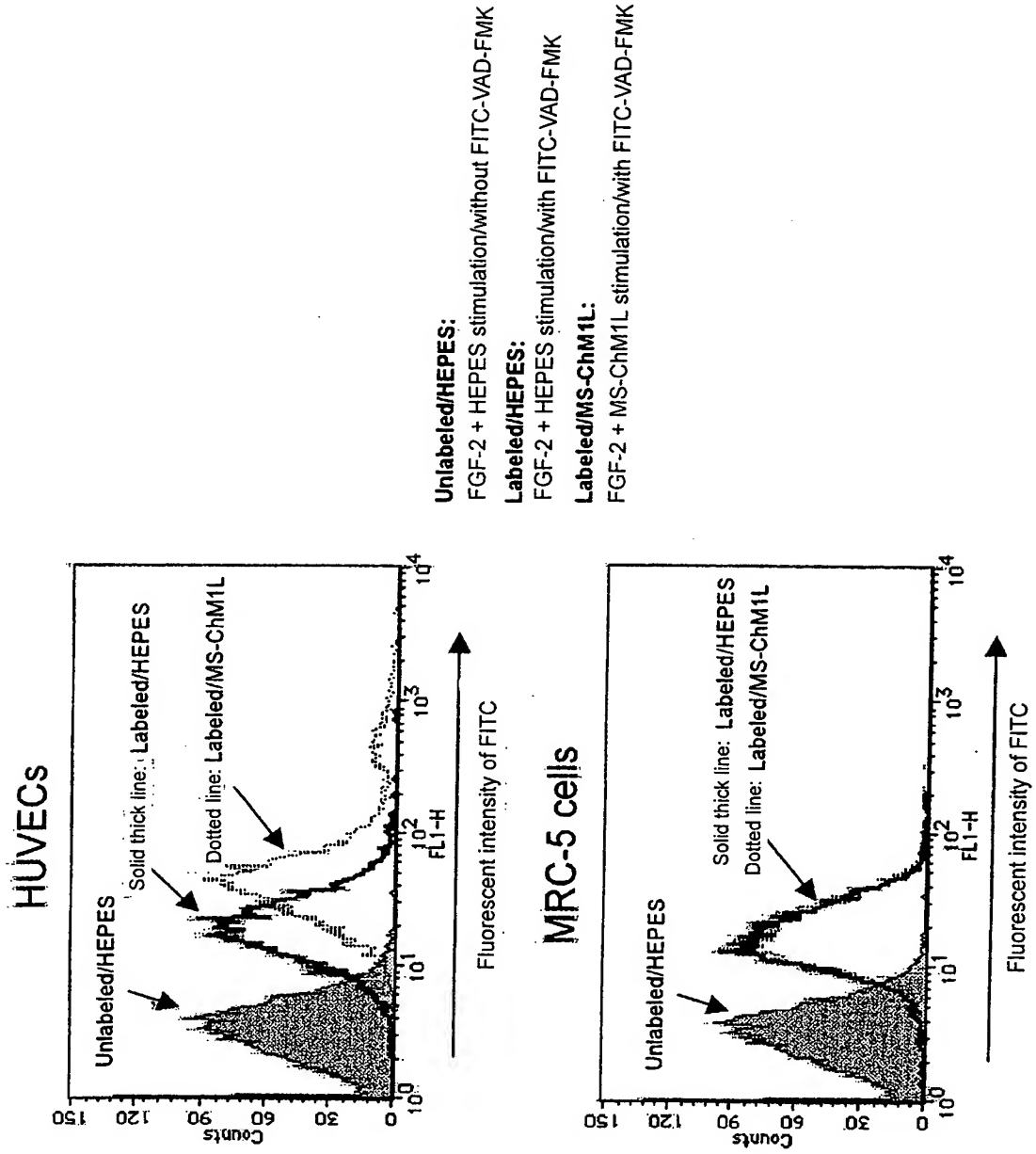

HUVECs
Unlabeled/HEPES
Solid thick line: Labeled/HEPES
Dotted line: Labeled/MS-ChM1L
Counts
FL1-H
Fluorescent intensity of FITC
MRC-5 cells
Unlabeled/HEPES
Solid thick line: Labeled/HEPES
Dotted line: Labeled/MS-ChM1L
Counts
FL1-H
Fluorescent intensity of FITC
Unlabeled/HEPES:
FGF-2 + HEPES stimulation/without FITC-VAD-FMK
Labeled/HEPES:
FGF-2 + HEPES stimulation/with FITC-VAD-FMK
Labeled/MS-ChM1L:
FGF-2 + MS-ChM1L stimulation/with FITC-VAD-FMK

Figure 23

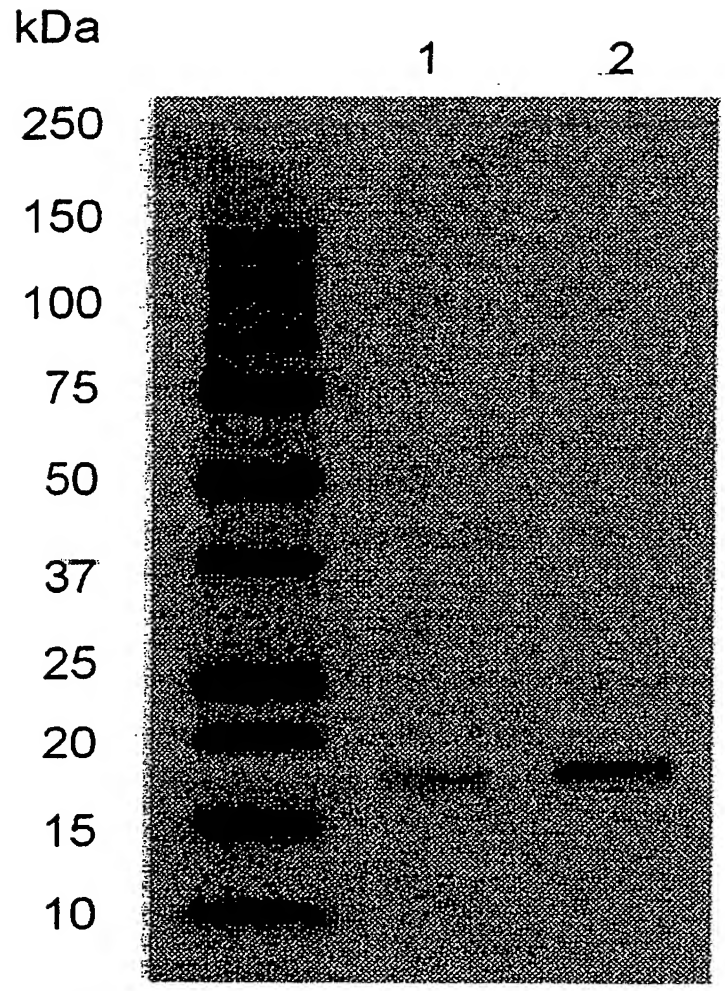


Figure 24

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.